REMARKS

Formal Matters

Claims 1-15, 18-23, 27, and 31-47, as well as new claims 48-52, are pending after entry of the amendments set forth herein.

Claims 1-23, 27, and 31-47 were examined. Claims 1-23, 27, and 31-47 were rejected. No claims were allowed.

Claims 16, 17, 26, 28, and 30 have been canceled.

Claims 1, 2, 4, 6-9, 11-13, 18-21, 31, 32, 36, 40, 44, and 47 have been amended. Support for the amendments can be found in the claims as originally filed and the specification at, for example, page 26, lines 22-26.

New claims 48-52 have been added. Support for new Claims 48-52 can be found in the claims as originally filed and throughout the specification at, for example: page 21, lines 14-26.

No new matter has been added.

Interview Summary

The Examiner is thanked for the telephonic interview held on September 13, 2005. During the interview, draft claims were discussed, as summarized in the Examiner's Interview Summary of September 22, 2005.

Withdrawal of Rejections and Objections

The Applicants express gratitude in the Examiner's indication that rejections and objections not reiterated from the previous Office Action have been withdrawn.

Objection to the Abstract

The abstract has been objected to for a typographical error. The abstract has been amended to correct the error in syntax and to recite "as well as the **encoded** proteins". Accordingly, this objection may be withdrawn.

Objections to the Specification

(a) Priority Information (Office Action page 3)

The specification has been objected to because the priority information on page 1 needs to be updated. In view of the amendment to the specification, this objection may be withdrawn.

(b) Sequence Identifier (office Action page 3)

The specification has been objected to for using an improper specific sequence identifier notation. In view of the amendment to the specification, this objection may be withdrawn.

(d) Title (Office Action page 3)

The title has been objected to for allegedly failing to describe the claimed invention. The title has been amended as suggested by the Examiner in the outstanding Office Action. Accordingly, this objection may be withdrawn.

Objections to the Claims

Claims 1-2, 8-9, 12-13, 16-21, and 40 (Office Action page 4)

Claims 1-2, 8-9, 12-13, 16-21, and 40 have been objected to because the species name in the claims is not italicized. Claims 1-2, 8-9, 12-13, 16-21, and 40 have been amend to italicize *Cnidarian*. Accordingly, this rejection may be withdrawn.

Claims 6, 7, 11, 16, 18, and 20 (Office Action page 4)

Claims 6, 7, 11, 16, 18, and 20 have been objected to for use of an improper sequence identification notation. The claims have been amended to correct the sequence identification notation. Accordingly, this rejection may be withdrawn.

Claims 6-7, 16, 18, and 20 (Office Action page 4)

Claims 6-7, 16, 18, and 20 have been objected to for use of "residues". Claims 6-7, 16, 18, and 20 have has been amended to remove the objectionable language. Accordingly, this rejection may be withdrawn.

Claim 31 (Office Action page 4)

Claim 31 has been objected to for lack of antecedent basis. Claim 31 has been amended to correct the antecedent basis. Accordingly, this rejection may be withdrawn.

Rejection Under 35 U.S.C. § 101

Claims 16-17 have been rejected under 35 U.S.C. § 101 for allegedly reading on a product of nature. Claims 16-17 have been canceled, rendering this rejection moot.

Rejection Under 35 U.S.C. §112, first paragraph (Written Description)

Claims 1-23, 27, and 31-47 have been rejected under 35 U.S.C. § 112, first paragraph, for allegedly lacking written description. This rejection is respectfully traversed.

In making this rejection, the Office Action asserts that "the claimed invention is directed to fragments, mutant and mimetics, which are not adequately described in the instant specification" (Office Action, page 6). In addition, the Office Action also states that claims 1-5, 8-10, 12-15, 22-23, 27, and 32 "are only defined by a function (encoding a protein)" (Office Action, page 6).

In the spirit of expediting prosecution and without conceding to the correctness of the rejection, the claims have been amended to remove the objectionable language and to recite that the **nucleic acids encode a protein that has an amino acid sequence that is at least 70% identical to the sequence of SEQ ID NO:12**.

The Applicants assert that the specification provides adequate written description support for such a claim. In particular, the Applicants respectfully submit that the specification provides abundant written description support for practicing the claimed invention. In particular, the Applicants note that the specification provides support for the subject nucleic acids at, for example, on page 8, line 11 through page 17, line 6; representative chromo- or fluorogenic proteins encoded by nucleic acids are described

at, for example, on page 9, line 12 though page 12, line 15; exemplary methods of producing and testing variants of the proteins at, for example, on page 13 line 20 through page 14, line 8, and in greater detail on page 39, line 13 through page 57, line 5; and resulting exemplary species of the claimed genus at, for example, in Table 10 on pages 56-57.

For example, the specification provides **at least ten different variants** of SEQ ID NO:12, including E5, E8, E5up, E5down, E57, AG4, AG45, FP6(E57)-NA, E5-NA, and E83. The sequences of the variants are further described at, for example, Figure 16 and page 47, line 35 to page 53, line 20. In addition, other examples of chromo- or fluorogenic proteins having at least a sequence identity of at least 70% with SEQ ID NO:12 are also provided in the specification, such as, for example, SEQ ID NO:18.

Furthermore the specification provides working examples demonstrating exemplary protocols for isolating the subject nucleic acids encoding the proteins, exemplary mutagenesis protocols, and exemplary methods of generating and testing such mutant peptides (Examples I-VIII, pages 38-56), and examples of variants generated (Table 10, pages 56-57).

In view of the above, it is submitted that the claims do comply with the written description requirement. The specification provides multiple representative examples, including working examples of representative nucleic acids encoding exemplary variant proteins, such that one of skill in the art would have no doubt that the applicant was in possession of the invention as claimed at the time the application was filed. Therefore, this rejection may be withdrawn.

Rejection Under 35 U.S.C. §112, first paragraph (Enablement)

Claims 1-23, 27, and 31-47 have been rejected under 35 U.S.C. §112, first paragraph, for allegedly failing to provide enablement for the claims. In view of the amendments to the claims, this rejection may be withdrawn.

In particular, the Office Action assert that the specification "does not reasonably provide enablement for any fragment, mutant or mimetic thereof or a transgenic organism or progeny thereof" (Office Action, page 8).

As noted above, the claims have been amended to remove the objectionable language and to recite that the nucleic acids encode a protein that has an amino acid sequence that is at least 70% identical to the sequence of SEQ ID NO:12.

The Applicants respectfully submit that the quantity of experimentation required to practice the subject invention is reasonable. The courts have clearly taught that the fact that experimentation may be complex does not necessarily make it undue, if the art typically engages in such experimentation. For example, see MPEP §2164.01.[1]

The Federal Circuit has found that even extensive experimentation is not undue in the molecular biology arts, particularly with respect to polypeptide variants. For example, the court concluded that extensive screening experiments to determine whether a polypeptide variant maintained a biological activity, while being voluminous, were not undue in view of the art which routinely performs such long experiments. The Federal Circuit stated:

> The claimed compositions recite isolated polypeptides with **60% or more sequence identity to SEQ ID NO:3** that suppress proliferation of lympho-hematopoietic cells. **The only experiments, if any, that need be performed to enable the entire scope of the claim are those designed to determine which sequences retain the ability to suppress proliferation of lympho-hematopoietic cells**. The sequence of polypeptides retaining biological activity is determined through routine experimentation that is empirical in nature, typically employing nothing more than performing the same assay disclosed in the specification on a variety of sequence variants of the polypeptide made by routine recombinant DNA techniques. **Since these experiments are empirical in nature, no undue experimentation is required.** In other words, the only experimentation that may be required to enable the claimed invention are those experiments to determine the

[1]. See also *In re Certain Limited-Charge Cell Culture Microcarriers*, 221 USPQ 1165, 1174 (Int'l Trade Comm'n 1983), *aff'd sub nom., Massachusetts Institute of Technology v. A.B. Fortia*, 227 USPQ 428 (Fed. Cir. 1985).

> presence of a certain activity, and since **this only requires a routine assay on polypeptide variants** to determine the active variants, **no undue experimentation is necessary**.[2]

(emphasis added).

The claims of present application are directed to nucleic acids encoding a chromo- or fluorescent protein from a non-bioluminescent Cnidarian species, where the protein has an amino acid sequence that is at least 70% identical to SEQ ID NO:12.

As in Hybritech, polypeptides according to the invention that retain the biological activity are "determined through routine experimentation that is empirical in nature, typically employing nothing more than performing the same assay disclosed in the specification on a variety of sequence variants of the polypeptide...Since these experiments are empirical in nature, no undue experimentation is required."[3] In particular, the polypeptides according to the invention that retain the chromo- or fluorescent property can be routinely determined as described in the specification at, for example, page 54, line 32 through page 55, line 34.

Moreover, the Applicants note that the specification provides guidance for the subject nucleic acids at, for example, on page 8, line 11 through page 17, line 6; proteins encoded by nucleic acids are described at, for example, on page 9, line 12 though page 12, line 15; and representative number of species within the claimed genus at, for example, in Table 10 on pages 56-57

For example, the specification provides at least **ten different variants** of SEQ ID NO:12, including E5, E8, E5up, E5down, E57, AG4, AG45, FP6(E57)-NA, E5-NA, and E83. The sequences of the variants are further described at, for example, Figure 16 and page 47, line 35 to page 53, line 20. In addition, other examples of chromo- or fluorogenic proteins having at least a sequence identity of at least 70% with SEQ ID NO:12 are also provided in the specification, such as, for example, SEQ ID NO:18.

---

[2] *Hybritech v. Monoclonal Antibodies, Inc.* 231 USPQ 81 (Fed. Cir. 1986)
[3] *Hybritech v. Monoclonal Antibodies, Inc.* 231 USPQ 81 (Fed. Cir. 1986)

Accordingly, the experimentation is not excessive, voluminous, or undue. Applicants respectfully submit that the specification provides ample guidance and direction, coupled with the information available in the relevant art, for one of skill to practice the claimed invention without undue and excessive experimentation. Therefore, in view of the amendments to the claims, this rejection may be withdrawn.

Rejection Under 35 U.S.C. §102(b)

The Office Action maintains the rejection of Claims 1-5, 8-10, 12-23, 27, and 31 under 35 U.S.C. § 102(b) for allegedly being anticipated by Anderluh et al. (Biochem. Biophys. Res. Comm., 220:437-442 (1996)). This rejection is respectfully traversed.

As noted previously, the wild-type Equinatoxin II protein disclosed in the cited references is not a **chromo- or fluorescent protein**. Any observed fluorescence is from individual tryptophan residues and not from a fluorophore. Therefore, Anderluh et al. and Macek et al. do not disclose a fluorescent protein, as defined in the relevant art.

However, in the spirit of expediting prosecution and without conceding as to the correctness of the rejection, the claims have been amended to recite that the protein have a sequence identity of at least 70% to the sequence of SEQ ID NO:12. Since the cited reference does not teach a protein having a sequence identity of a lest 70% to the sequence of SEQ ID NO:12, the cited reference does not teach each and every limitation found in the claims.

As such, Claims 1-5, 8-10, 12-23, 27, and 31 are not anticipated under 35 U.S.C. § 102(b) by the cited reference. Therefore, the Applicants respectfully request that this rejection be withdrawn.

CONCLUSION

In view of the above remarks, this application is considered to be in good and proper form for allowance and the Examiner is respectfully requested to pass this application to issuance.

The Commissioner is hereby authorized to charge any underpayment of fees associated with this communication, including any necessary fees for extensions of time, or credit any overpayment to Deposit Account No. 50-0815.

Respectfully submitted,
BOZICEVIC, FIELD & FRANCIS LLP

Date: September 27, 2005

By: _____
Bret E. Field
Registration No. 37,620

BOZICEVIC, FIELD & FRANCIS LLP
1900 University Avenue, Suite 200
East Palo Alto, CA 94303
Telephone: (650) 327-3400
Facsimile: (650) 327-3231

F:\DOCUMENT\CLON\035cip\response to office action of 7-6-05.DOC